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Combined Effect of Botulinum Toxin Type A Injection and Intensive Occupational Therapy in Treatment of Spastic Pronators in Children with Cerebral Palsy

Sanne S.L. Fong[1], Kwok Bun Tam[2], Catherine K.Y. Fung[1], Vivian W.Y. Chui[1], Stella W.C. Cheng[1], Grace S.F. Ng[3], Teresa Y.L. Wong[3] and Kwok Yin Chan[3]

Objective: Botulinum toxin type A (BtA) injection in the therapeutic treatment of muscle hypertonicity has been documented to reduce spasticity in specific muscle groups, with the effect lasting 1–3 months. The objective of this study was to evaluate the combined effect of an intensive occupational therapy (OT) programme following BtA injection in the treatment of spastic pronators in children with cerebral palsy.
Methods: This study used a pre/post intervention measurement design. Five children with cerebral palsy and hand function impairment were enrolled for intervention and followed-up longitudinally at 1, 3, 6 and 12 months. All patients received BtA injection to left pronators followed by OT according to treatment guidelines and standard assessment protocol. Outcome measures included change in spasticity, active range of motion (AROM), sensibility, power grip strength and functional hand grips.
Results: Significant improvements in muscle tone, AROM, sensibility and functional hand grips were observed over time. The restoration of hand function and sensibility lasted up to 12 months after injection. In addition, we observed that four children gained sensibility, which did not demonstrate any tendency to diminish with time.
Conclusion: A combination of BtA injection and OT is effective for reducing spasticity in the pronators of children with cerebral palsy.

KEY WORDS: Botulinum toxin injection • Cerebral palsy • Occupational therapy • Spastic pronators

Introduction

Children with cerebral palsy (CP) usually present with typical deformities that include elbow flexion, forearm pronation, thumb adduction in palm, wrist flexion and ulnar deviation, which limit the normal exploration of their environment. In children with CP, the spasticity due to upper motor neuron lesion can interfere with mobility, self-care, positioning, and will sometimes lead to deformities. Ruthman (1986) compared CP children with their normal counterparts with regard to the influence of impaired mobility on acquisition of one aspect of cognition development; the results suggested that ordering movements might be limited in children with CP as a result of their limited motor experience, particularly at a young age. On the other hand, Cooper, Majnemer, Rosenblatt, and Birnbaum (1995) reported that 30–97% of patients with CP have defective stereognosis. Any intervention that will allow more efficient use of the spastic hand should therefore lead to an improvement in stereognosis. Dahlin, Salgeback, Komoto-Tufvesson, and Lundborg (1998) suggested that the brain areas for reception of afferent impulses may be downregulated as a result of non-use of the hands, but stereognosis can be improved following surgical reconstruction of the upper extremity in patients with CP due to functional cerebral reorganization induced by the modified afferent inflow.

Departments of [1]Occupational Therapy, [2]Orthopaedics and Traumatology, and [3]Paediatric and Adolescent Medicine, Princess Margaret Hospital, Hong Kong SAR, China.
Reprint requests and correspondence to: Miss Sanne S.L. Fong, Department of Occupational Therapy, Princess Margaret Hospital, Kwai Chung, Hong Kong SAR, China.
E-mail: fongsl@ha.org.hk

They studied 36 patients with hemiplegic CP who were treated with various surgical means of tendon transfer to improve or correct their supination, wrist extension or the thumb-in-palm deformity, which was then followed by comprehensive hospital-based occupational therapy (OT). They observed improvements in stereognosis.

Botulinum toxin type A (BtA) injection has been used in the treatment of hemiplegic upper limb muscle hypertonicity in children with CP. Local intramuscular injection of BtA assisted in reducing disability and enhanced functional improvements, having a high impact on the activities of daily living and on quality of life (Mall, Heinen, Linder, Philipsen, & Korinthenberg, 1997). Intramuscular injection of BtA is believed to be a safe and effective measure for relieving spasticity in paediatric CP patients, to diminish painful spasticity, to facilitate positioning and hygiene, to improve ambulation and upper limb function, and to be a useful diagnostic aid in determining the efficacy of surgery. Suputtitada (2000) indicated that a very low dose of BtA combined with rehabilitation therapy resulted in a long-lasting decrease in spasticity and an improvement in gait in children with CP. There is much in the literature on the basic principles of the mode of action, side effects, therapy failure, and potency comparison of BtA and its clinical applications to dystonia and spastic conditions in children with CP (Borodic, Ferrante, Pearce, & Smith, 1994; Lagalla, Danni, Reiter, Ceravolo, & Provinciali, 2000; Lee & Powell, 1990; Yasukawa, 1990). However, it has been generally reported that the effects last for only about 3 months (Corry, Cosgrove, Walsh, McClean, & Graham, 1997; Graham, 2000).

Eliasson (1995) wrote that functional hand movements in daily life are built up by motor sequences related to sensory, perceptual, and cognitive functions. Most children with CP have no functional sensorimotor integration during the grasping task as their force generation is usually unstable, which will affect their handling of objects. Moreover, their anticipatory control is poor and they cannot rely on stable force generation or efficient sensory feedback to generate an effective force. By altering the muscle tone with BtA injection, function can be enhanced or additional therapeutic modalities can be employed. Hence, BtA injection followed by an intensive rehabilitation programme with repetition of goal-directed activities can lead children with CP to experience a process of progressive adjustment and master a skilled movement (Russman, Tilton, & Gormley, 1997).

An OT rehabilitation programme will usually include splinting as a type of environmental intervention. Static splints that can provide maximum extension and/or abduction stretch beyond the point of spasticity can prevent deformity and contracture resulting from spasticity (Spencer, 1983). Preston (2004) suggested that the use of serial casting and static splints (6–8 hours/day) can maintain range of motion. In this study, we hypothesized that serial splinting as a home programme in addition to intensive functional training conducted by occupational therapists in adjunct with BtA injection therapy can optimize the effect of BtA treatment in the reduction of spasticity and improvement of hand function in children with CP. Specifically, the objective of this study was to investigate the effectiveness of a combination of BtA injection and OT programme for children with CP in the acquisition of hand grasp control.

Methods

This study used a pre/post intervention measurement design with longitudinal follow-ups at 1 month, 3 months, 6 months and 12 months. Five patients were recruited from a bimonthly, multidisciplinary Paediatric Hand Clinic in an acute hospital between August 2002 and July 2005. The demographic characteristics of the patients are shown in the Table. The clinic is jointly run by an orthopaedic surgeon, paediatric neurologists and occupational therapists. The inclusion criteria for the patients to be enrolled in the study were: (1) presence of spastic pronators with good rehabilitation potential; (2) reasonable intelligence; (3) supportive family; (4) strong motivation to use the affected hand; (5) willingness to follow intensive treatment and assessment programme; and (6) good compliance with the splinting programme. All patients were followed-up

Table. Patients' demographic characteristics

Patient	Gender	Diagnosis	Age (yr)	BW (kg)	Muscle injected
1	Male	Triplegia Lt > Rt	10.5	35	Lt PQ; Lt PT
2	Female	Triplegia Lt > Rt	8.5	18	Lt PT; Lt Br; Lt FCU
3	Female	Lt hemiplegia	4	12.8	Lt PT
4	Female	Lt hemiplegia	5	19.6	Lt PT
5	Female	Rt hemiplegia	7	20.8	Rt PT

BW = body weight; Lt = left; Rt = right; PQ = pronator quadratus; PT = pronator teres; Br = brachialis; FCU = flexor carpi ularis.

longitudinally for up to 12 months and all had received BtA injection to the left pronator teres and/or pronator quadratus. A standard assessment protocol and treatment guidelines were established to ensure that the patients would benefit from optimal rehabilitation after BtA injection.

Botulinum Toxin Type A (BtA) Injection

BtA (DYSPORT, Ipsen Pharmaceuticals, France) was reconstituted for injection using 200–500 U for large muscles, and 100–300 U for small muscles. The dosage was calculated with reference to recommendations from the literature and the manufacturer according to the body weight of the patients, with the maximum dose being 20–25 U/kg body weight. The pronator teres or pronator quadratus was identified by an experienced orthopaedic surgeon, and all injections were given by the same surgeon. Injection was delivered with a 2.5-mL syringe using a 25-gauge needle to reduce pain and to minimize muscle trauma and bleeding. During injection, each patient was asked to sit and rest their forearm on the table or to lie supine on the bed to make sure that he/she could adopt a comfortable and relaxed position.

Occupational Therapy (OT) Programme

After injection, all patients were put on an OT programme. Treatment by occupational therapists included prescription of a forearm supination splint and intensive training for hand grasp and release and dexterity, as well as a strengthening and sensory reeducation programme. Standardized OT treatment guidelines were established to ensure that the patients would benefit from optimal rehabilitation after BtA injection. Within 1 week after injection, an occupational therapist would fabricate a forearm supination splint with thermoplastic material at 60–70°C to keep the forearm in maximal supination (Figure 1). All patients needed to wear the splint for 8–12 hours per day when asleep. The programme also included a weekly training session with remedial activities to develop hand function and sensibility, and to strengthen power grip and pinch grip (Appendix). The intensive training lasted for 2 months, after which the number of training sessions was reduced to once every 2 weeks (same as before the patients received the BtA injection).

Assessment

Assessments included: (1) active range of motion (AROM) as measured by a goniometer; (2) spasticity as measured by the Modified Ashworth Scale (Bohannon & Smith, 1987); (3) functional hand grips (Eliasson, Ekholm, & Carlstedt, 1998); (4) grasp and release of a film capsule (Corry et al., 1997); (5) sensibility as represented by stereognosis performance; (6) quality of hand function as measured by the Jebsen-Taylor

Figure 1. *A forearm supination splint.*

Hand Function Test (Jebsen, Taylor, Trieschmann, Trotter, & Howard, 1969); and (7) power grip strength as measured by a dynamometer. For functional hand grips, there were nine items studying transverse grasp, diagonal grasp, five-finger pinch, tripod pinch, lateral pinch, and tip to tip pinch with grading from 0 to 4 for each grip according to how well the child performed. Based on a total score of 36, children were ranked according to their individual score, ranging from severe impairment (≤ 13), to moderate impairment (14–21), to mild impairment (≥ 22) (Eliasson et al.). All patients were evaluated at baseline (pre-injection), and then post-injection at 1, 3, 6 and 12 months. In order to avoid assessment bias, all patient assessments were done and documented by the same occupational therapist, with video and photographic recording for subsequent review and analysis by another occupational therapist who confirmed the assessment results.

Results

Active Range of Motion (AROM)

There was an increase in active supination (Figure 2) and wrist extension (Figure 3) of the hands at 1, 6 and 12 months after injection. There was an average increase of 60° in supination. However, there was not much change in active pronation range and elbow range (Figures 4 & 5).

Change in Spasticity

In the first month after injection of BtA into the pronator teres and/or pronator quadratus, the muscle tone of the pronators

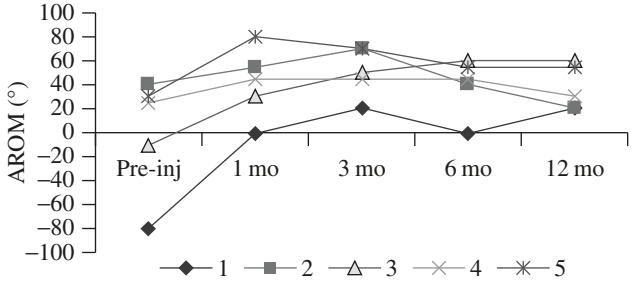

Figure 2. *Change in active range of motion (AROM) of forearm supination in the five patients. Pre-inj = pre-injection.*

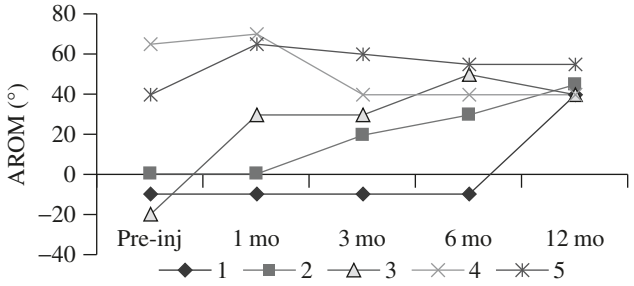

Figure 3. *Change in the active range of motion (AROM) of wrist extension in the five patients. Pre-inj = pre-injection.*

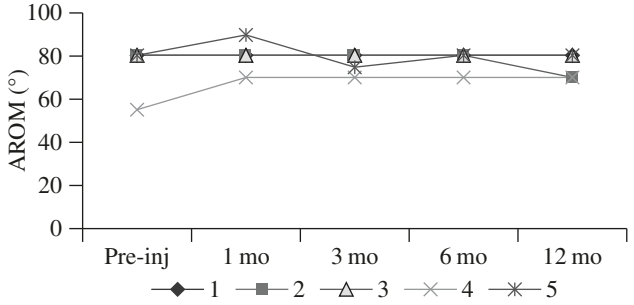

Figure 4. *Change in the active range of motion (AROM) of forearm pronation in the five patients. Pre-inj = pre-injection.*

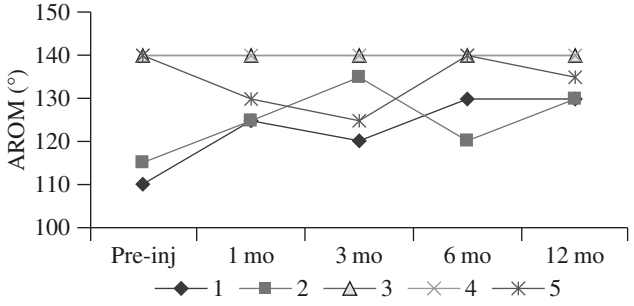

Figure 5. *Change in the active range of motion (AROM) of the elbow in the five patients. Pre-inj = pre-injection.*

was reduced from 1^{+}–3 to 1–2 (Figure 6), and that of the wrist flexors was reduced from 1–2 to 0–2 (Figure 7), according to the Modified Ashworth Scale. The effect lasted until 6 months after injection. The reduction in the degree of abnormal muscle

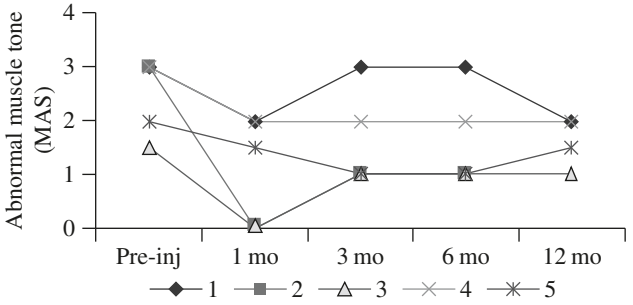

Figure 6. *Change in the spasticity of forearm pronators in the five patients. Pre-inj = pre-injection.*

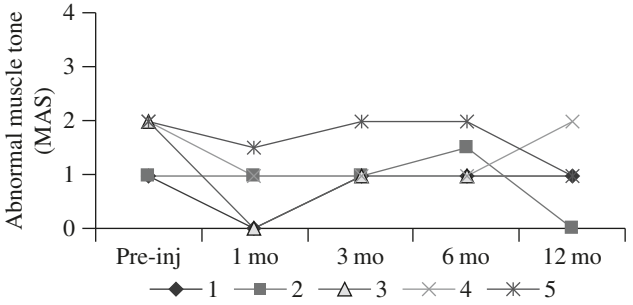

Figure 7. *Change in spasticity of wrist flexors in the five patients. Pre-inj = pre-injection.*

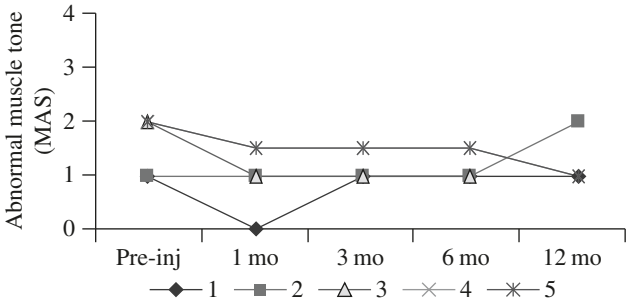

Figure 8. *Change in spasticity of elbow flexors in the five patients. Pre-inj = pre-injection.*

tone of the pronator teres and pronator quadratus had also lessened the tension of other muscles. Since the action of the pronator teres includes pronation of the forearm and flexion of the elbow, with release of the pronator teres, there was improvement in the muscle tone of the elbow flexors (Figure 8).

Functional Hand Grips

Mean functional hand grip increased gradually from 14.6 (range, 1–22) before injection to 24.4, 26.0, 24.8 and 24.0 at months 1, 3, 6 and 12 after injection, respectively. It was observed that functional hand grip improved dramatically within the first month, then gradually slowed down to a plateau or was reversed by 6 months (Figure 9). However, in general, overall score was better at 6 months. Among the five patients,

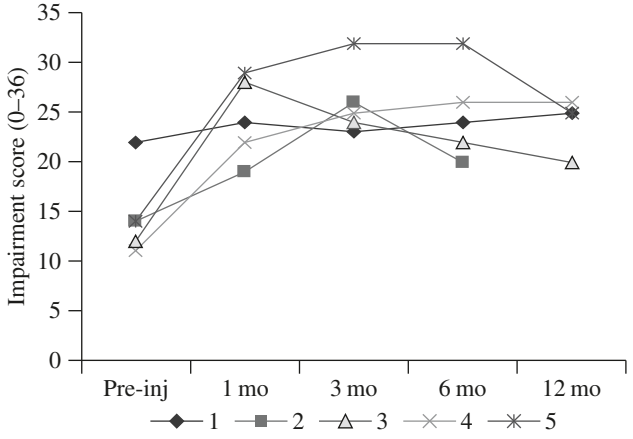

Figure 9. *Change in functional hand grip performance in the five patients. Pre-inj = pre-injection.*

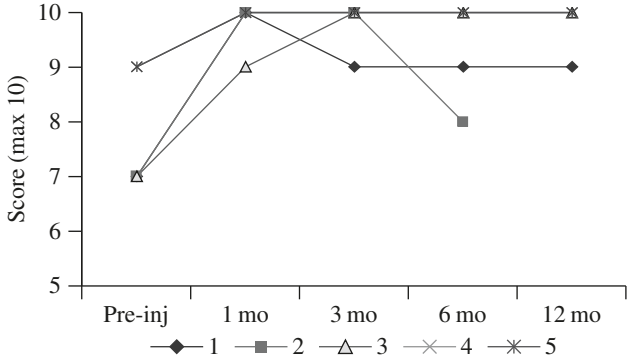

Figure 10. *Change in grasp and release performance of a film capsule in the five patients. Pre-inj = pre-injection.*

two had improved from severe to mild and another two had improved from moderate to mild, while one patient received an additional injection 9 months after the first injection.

Grasp and Release

All patients had improvement in the grasp and release pattern of a film capsule for a mean of 1.3 units of scoring with better posture. Only one patient needed an additional injection 9 months after the first injection (Figure 10) to enhance the grasp and release action.

Sensibility

With the improvement in muscle tone and further improvement in dexterity enabling the patients to further explore different objects, an overall improvement in stereognosis was noted. One year after injection and the rehabilitation programme, four patients were still maintaining their gained skills in stereognosis and were able to discriminate 11–14 objects in the stereognosis kit (Figure 11).

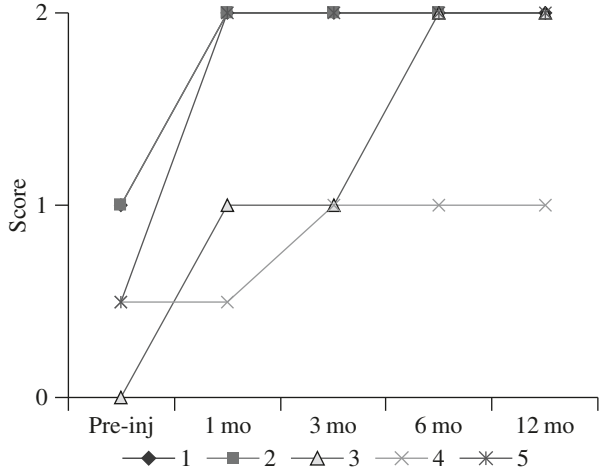

Figure 11. *Change in stereognosis in the five patients. Pre-inj = pre-injection.*

Quality of Hand Function

With improvement in the quality of hand function, patients could perform more sophisticated hand tasks. The Jebsen-Taylor Hand Function Test was used to assess the speed of completing seven hand functional tasks. Most patients showed improvement in the efficiency of picking up small objects, stacking checkers and turning cards. However, the changes in tasks that demanded active supination of the forearm and stabilization of the wrist such as controlling a spoon during simulated feeding, turning cards and controlling a pen during writing were not obvious. None of the patients could pick up large and heavy objects, which demands a wide span and strong wrist stabilization.

Power Grip Strength

The mean grip strength was 3.0 kgf before injection and was 1.85 kgf, 2.3 kgf, 2.1 kgf and 2.625 kgf in months 1, 3, 6 and 12 after injection, respectively. Grip strength measured before BtA injection was probably a result of hypertonicity rather than an actual functional strength. Hence, it was not a surprising finding that after BtA injection, grip strength was apparently reduced. It was expected that grip strength dropped in the first month, and then when abnormal muscle tone returned, apparent grip strength increased again (Figure 12).

Discussion

After injection of BtA, the spasticity of the pronator teres and/or pronator quadratus was reduced, and the active range of wrist extension and supination improved. There was also relief in the tension of the joint capsule of the wrist joint. Hence, active participation in rehabilitation was facilitated, and proprioception and stereognosis were enhanced. This, in turn,

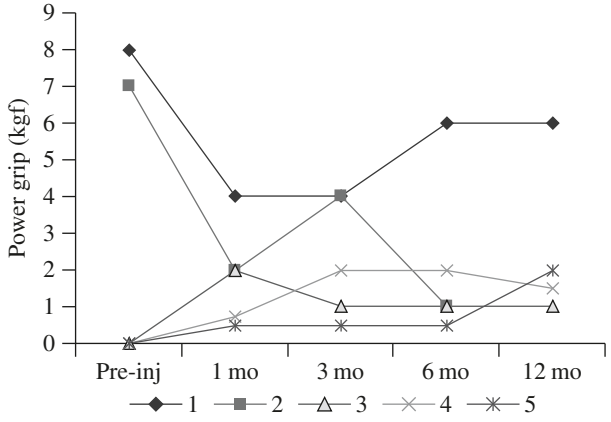

Figure 12. *Change in power grip strength in the five patients. Pre-inj = pre-injection.*

facilitated motor learning for normal movement pattern of hand functions. All patients developed a more efficient grasp and release pattern with better posture, such as picking up small objects and turning cards. Functional hand grip improved and lasted longer than expected after the effects of BtA subsided.

The reduction in the degree of abnormal muscle tone of the pronator teres and/or pronator quadratus also lessened the tension of other muscles, although we could not exclude the possible diffusion effect of BtA to other muscles upon injection. With improvements in muscle tone and dexterity, patients had more opportunity to explore different objects, which led to an overall improvement in stereognosis. From our observations, younger patients had better functional reorganization of the somatosensory cortex of the brain compared to older patients, and were thus able to learn the sensibility better after BtA injection, and no deterioration was noted after this gain. Krumlinde-Sundholm and Eliasson (1993) studied 25 children with spastic hemiplegia and found that spasticity and deficient sensibility were significantly correlated with dexterity of the hemiplegic hand. It was believed that there was functional reorganization of the somatosensory cortex of the brain as a result of changes in afferent input from the hand. In our study, patients with less severe functional impairment improved better as the area in the brain for reception of afferent impulses was not completely downregulated, i.e. less severe impairment in hand function facilitated functional cerebral reorganization by modified afferent inflow during sensory education.

The measured grip strength before injection was actually a measure of grip strength due to hypertonicity. Therefore, grip strength was reduced significantly after injection, and the gradual restoration of grip strength to lower than pre-injection levels reflected that actual grip strength might be weaker. This indicated that more strengthening elements to both agonist and antagonist should be offered in the training programme. The optimal time for training of muscle strength lay between 1 and 6 months after injection. Before the injected muscle returned to its hypertonic state, the antagonist could gain a certain degree of strength so as to retain control of the affected hand. Duff and Gordon (2003) suggested that practice sessions should incorporate lifts with novel objects to enhance anticipatory force scaling and related prehensile function in children with hemiplegic CP.

In summary, our study produced similar results as that seen in other countries. Our patients lost muscle strength and had compromised hand function in the first month, but they gradually improved in muscle strength, AROM, and hand functions to a maximum by 3 months. This pattern was consistent with the results of other similar studies. In addition, we also observed that four out of the five patients gained sensibility, which had no tendency to diminish with time.

Furthermore, better results were noted in the younger patients, those who had disabilities without contracture, reasonable intelligence, and very good family support, as well as those with specific hand tasks to achieve before injection, and those who demonstrated good compliance with the rehabilitation programme. All these factors contributed to the success of the BtA injection and these types of patients were expected to benefit most from our intervention.

Lastly, the patients were able to learn sensibility after BtA injection. The injection had broken a vicious cycle and enhanced the development of sensibility and the motor learning process. Sensory information (Eliasson, 1995; Eliasson et al., 1998) was important in learning movements; the sensory signals corrected and adjusted the movements and updated the motor programme for correct execution the next time the programme was used. The patient who would benefit most from BtA treatment is the one who is hypertonic and whose abnormal muscle tone is interfering with function, or who is expected to develop joint contracture with growth because of this abnormal tone. By altering this muscle tone, function can be enhanced or additional therapeutic modalities can be employed (Russman et al., 1997).

In this study, an intensive OT programme was implemented after BtA injection. The effect of this combined treatment lasted for at least 6 months. The provision of intensive training and patients' compliance with the splinting programme contributed to postpone the reversal of the effects of BtA injection. Hence, patients could maintain a prolonged effect and the timing of optimal functioning was able to be maximized as compared with other similar studies.

There were limitations in this study. Only five patients were recruited, which obviously limits the generalizability of the study results. It was also difficult to recruit patients who were treated with BtA injection alone without the use of any other

kind of intervention, so we could not compare the effects of combined treatment with the effects of BtA injection alone.

Conclusion

BtA injection should not be used alone. Instead, injection of BtA to the extensors should be followed-up by an intensive OT programme, with emphasis on the development of sensation and strengthening of wrist joint muscles. There was evidence that the success of surgery correlated very closely with good preoperative stereognosis training (Zancolli & Zancolli, 1990). We also recommend a course of intensive sensory reeducation and motor learning to children with CP after any BtA injection before reconstructive hand surgery is considered.

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Appendix. Occupational Therapy Protocol for Spastic Hand Treatment After Botulinum Toxin Type A Injection

Aims

- To monitor and maximize hand function after injection
- To provide a splinting programme to prevent deformities, and to improve and facilitate hand function and development
- To encourage usage of the affected hand and facilitate development of normal movement pattern in daily activities
- To provide regular training with the residual ability of the spastic hand

<table>
<tr><td></td><td>Assessment schedule</td><td></td><td colspan="2"></td></tr>
<tr><td>Before intervention</td><td colspan="4">Hand function assessment to document baseline condition
Give suggestion for injection, and set aims for patients and/or relatives, the neurologist and orthopaedic surgeon in clinic</td></tr>
<tr><td></td><td></td><td>Training</td><td colspan="2">Splinting and regimen</td></tr>
<tr><td>Injection</td><td></td><td></td><td colspan="2"></td></tr>
<tr><td rowspan="2">Wk 1
↓
Wk 4</td><td rowspan="2"></td><td rowspan="2">Start weekly intensive training for 1st mo:
• Upper limb weight-bearing activities 2 meters × 10 repetitions
• Activities to improve AROM beyond limit and encourage development of normal movement patterns
• Hand function training
• Self-care training</td><td colspan="2">Static splint to provide maximum and tolerable stretching of involved muscle within the 1st mo
Whole day resting splint, off except for functional training during wk 1–2</td></tr>
<tr><td>Night splint
Resting splint to provide maximal stretching (may need to adjust serially to patients' tolerance) of injected muscles</td><td>Day splint
Provide functional support and facilitate hand function training</td></tr>
<tr><td></td><td colspan="4">Assessment 1 mo after injection</td></tr>
<tr><td rowspan="2">Mo 1
↓
Mo 3</td><td rowspan="2"></td><td rowspan="2">Continue weekly intensive training for another month, add strengthening activities
for injected muscles and antagonists:
• Upper limb weight-bearing activities 2 meters × 10 repetitions
• Activities to encourage AROM
• Grip & pinch strengthening
• Activities that encourage bilateral coordination, then response speed
• Encourage functional grasp</td><td colspan="2">Keep night static splint
Home programme encouraged</td></tr>
<tr><td>Night splint (~ 8 hr/d)
Resting splint to provide maximal stretching of injected muscles</td><td>Day splint
May consider dynamic approach if indicated
• Cock-up splint to stabilize wrist joint for grasp & release
• Thumb spica to stabilize 1st MCPJ for hand function training</td></tr>
</table>

<table>
<tr><td></td><td colspan="4">Assessment 3 mo after injection
Gradual wean off treatment to previous biweekly basis if condition maintained well; if deterioration noted, investigate the reason in clinic for further management</td></tr>
<tr><td rowspan="2">Mo 3
↓
Mo 6</td><td rowspan="2"></td><td rowspan="2">Gradual wean off to biweekly training:
• Upper limb weight-bearing activities 2 meters × 10 repetitions
• Activities to encourage normal movement patterns
• Grip & pinch strengthening
• Functional tasks training</td><td colspan="2">Keep night static splint
Home programme encouraged</td></tr>
<tr><td>Night splint (~ 8 hr/d)
Resting splint to provide maximal stretching of injected muscles</td><td>Day splint
• Cock-up splint to stabilize wrist joint for grasp & release
• Thumb spica to stabilize 1st MCPJ for hand function training</td></tr>
<tr><td></td><td colspan="4">Assessment 6 mo after injection
• If condition is well kept, continue night splint, home programme and biweekly training for maintenance, then re-evaluate at 12 mo
• Consider repeat intervention if condition has reversed and resume weekly training upon decision in clinic</td></tr>
<tr><td rowspan="2">Mo 6
↓
Mo 12</td><td rowspan="2"></td><td rowspan="2">Gradual wean off to biweekly training:
• Upper limb weight-bearing activities 2 meters × 10 repetitions
• Activities to encourage normal movement patterns
• Grip & pinch strengthening
• Functional tasks training</td><td colspan="2">Keep night static splint
Keep home programme</td></tr>
<tr><td>Night splint (~ 8 hr/d)
Resting splint to provide maximal stretching of injected muscles</td><td>Day splint
• Cock-up splint to stabilize wrist joint for grasp & release
• Thumb spica to stabilize 1st MCPJ for hand function training</td></tr>
<tr><td></td><td colspan="4">Assessment 12 mo after injection
• Keep night static splint and home programme
• If condition is well kept, continue biweekly training for maintenance
• If mildly reversed condition is noted, consider re-injection to facilitate further improvement of hand function, but only if child is motivated to improve his/her quality of life/hand function
• According to assessment of hand function and abnormal muscle tone, spasticity will usually return to the previous level and limit activities of daily living
• Liaise with case physician if condition reverses or even becomes out of control; look for indications of further intervention</td></tr>
</table>

AROM = active range of motion; MCPJ = metacarpophalangeal joint.

Notes:
1) Injection of Dysport/Botox will result in a transient and reversible effect.
2) If the result is satisfactory, look for a ceiling effect of multiple injections of Dysport/Botox; phenol block may be considered as an alternative.
3) If deformity is severe and fixed contracture is present, and hypertonicity is not generally affecting the patient, surgery is the final option.